AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,085	10/07/2002	Naoshi Fukushima	065678-0108	7376

22428 7590 11/17/2005

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,085	FUKUSHIMA ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-22 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature recited in claim 1 is an antibody containing the H and L variable regions of a monoclonal antibody, and capable of binding a cell-surface antigen(s) to produce an agonist effect. In view of this, Mateo et al. (Nature Medicine, 5:1277-1284, November 1999; cited in the IDS of April 29, 2003) reads on the claim. Mateo et al. (see p. 1279, Col. 1, line 6- Col. 2, line 3) teach that cross-linking of a cell-surface receptor (CD 47 antigen) by two monoclonal antibodies of different isotype specificity produced an agonist effect (inducing apoptosis in a B-cell line). Further, Mateo et al. teach that modified antibodies, Fab and F(ab)2 fragments for anti-CD 47 monoclonal antibodies, induce apoptosis (Figure 3e). Thus, the reference anticipates the invention because Mateo et al. teach modified antibodies producing agonist effects upon cross-linking of cell-surface receptors. Therefore the technical feature recited in claim 1 is not special. Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s)1-13, drawn to a polypeptide (monoclonal-derived modified antibody).

Group II, claim(s) 14-16, drawn to a polynucleotide and host cells.

Group III, claim(s) 17, drawn to a method of treatment using a hybrid antibody.

Group IV, claim(s) 18, 19, drawn to a method for producing and stabilizing a Fv dimer.

Group V, claim(s) 20-22, drawn to a method for inducing an effect in a cell with a first and second ligand.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: As set forth above, in view of the teaching of Mateo et al and US Patent 4,946,788, the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature of claim 1 is not special.

The polypeptides Group I and the DNA of Group II are related. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function or effect. See MPEP § 806.05(j). In the instant case, the DNA claims do not overlap the scope of the polypeptide claims and vice versa as evidence by the distinct structures and functions of the claimed inventions. A DNA's structure is comprised of linear, contiguous nucleotides while a protein's

structure comprised of linear, contiguous amino acids that fold into a specific three-dimensional structure; the DNA's function is to encode a protein while a protein's function is variable, and in this case, the antibody should act as an agonist for a cell-surface receptor. Additionally, the DNA and polypeptides are not obvious variants of each other based on the distinct structures and functions of each as noted above. Lastly, the DNA and polypeptides have materially different functions as noted above.

To search Groups I and II together would present a search burden on the Examiner due to the extensive databases of non-patent literature. Thus, Groups I and II have been appropriately restricted on the basis of being both independent or distinct and presenting a search burden on the Examiner if they were to be searched together.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the modified antibody of Group I can be used in a materially different method such as to purify it's cognate antigen in addition to the materially different method of Group III. Additionally, the method of using an agent to provide an agonist effect through receptor cross-linking has been achieved using agents other than hybrid antibodies (e.g., ligand/receptor photoaffinity conjugation, ligand/receptor disulfide crosslinking).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject

matter and different searches in the patent literature, restriction for examination purposes as indicated is proper.

Inventions I and IV are related as product made and process of making. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the case of the process, other single chain proteins can be expressed by animal host cells that have been transformed with recombinant vectors encoding the single chain proteins, and which proteins form dimers through a linker. For example, a protein may be a bivalent peptide ligand consisting of a ligand domain, a spacer and linker for dimerization, wherein the ligand domain is alpha-melanocyte stimulating hormone. In the case of the antibody product, an insect cell or bacterial cell expression system can be used to produce the Fv monomers, or Fv monomers could be synthesized by solid-phase peptide synthesis.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process is so broad, that it encompasses any first and second ligand being cross-linked to transduce an agonist action through a cell surface molecule. Such first and second ligands may be two natural and different ligands binding to their respective cell surface receptor(s).

Alternatively, a single receptor may have two different natural ligands, which can be cross-linked to transduce a signal. In the foregoing examples, the ligands need not be hybrid antibodies much less Fv monomers. In the case of the hybrid antibody, the antibody could be used in immunoassays for detecting an antigen or in purifying an antigen.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and different searches in the patent literature, restriction for examination purposes as indicated is proper.

The methods of Inventions III-V differ in the method objectives, method steps and parameters and in the reagents used. Invention III recites treating with a hybrid antibody through an agonist effect; Invention IV recites expressing monomeric chains of an antibody to produce a hybrid antibody; and Invention V recites producing an agonist effect in a cell by cross-linking two ligands for a cell surface receptor(s). The examination of all groups would require different searches in the U.S. PATENT shoes and the scientific literature and would require the consideration of different patentability issues. Thus Inventions III-V are separate and distinct in having different method steps and different endpoints and are patentably distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and different searches in the patent literature, restriction for examination purposes as indicated is proper.

If Group I is elected, then species below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

A) erythropoietin receptor (EPO)

B) thrombopoietin receptor (TPO)

C) granulocyte colony stimulating factor (G-CSF) receptor

D) macrophage colony stimulating factor (M-CSF) receptor

E) granular macrophage colony stimulating factor (GM-CSF) receptor

F) tumor necrosis factor (TNF) receptor

G) interleukin-1 (IL-1) receptor

H) interleukin-2 (IL-2) receptor

I) interleukin-3 (IL-3) receptor

J) interleukin-4 (IL-4) receptor

K) interleukin-5 (IL-5) receptor

L) interleukin-6 (IL-6) receptor

M) interleukin-7 (IL-7) receptor

N) interleukin-9 (IL-9) receptor

O) interleukin-10 (IL-10) receptor

P) interleukin-11 (IL-11) receptor

Q) interleukin-12 (Il-12) receptor

R) interleukin-13 (IL-13) receptor

S) interleukin-15 (IL-15) receptor

T) interferon-alpha (IFN-alpha) receptor

U) interferon-beta (IFN-beta) receptor

V) interferon-gamma (IFN-gamma) receptor

W) growth hormone (GH) receptor

X) insulin receptor

Y) blood stem cell proliferation factor (SCF) receptor

Z) vascular epidermal growth factor (VEGF) receptor

AA) epidermal cell growth factor (EGF) receptor

BB) nerve growth factor (NGF) receptor

CC) fibroblast growth factor (FGF) receptor

DD) platelet-derived growth factor (PDGF) receptor

EE) transforming growth factor-beta (TGF-beta) receptor

FF) leukocyte migration inhibitory factor (LIF) receptor

GG) ciliary neurotrophic factor (CNTF) receptor

HH) oncostatin M (OSM) receptor

II) Notch family receptor

The inventions can be shown to be distinct if both of the following can be shown: (1) the species are mutually exclusive and (MPEP 806.04(f)) and (2) not obvious alternatives (MPEP 803.02). Species A-II are patentably distinct because each of the species recites limitations not found in the other and the species do not have a commonality of operation, function or effect.

Species B-V, X, Y, FF and HH are CD antigens, each well recognized in the art as being expressed on different cell types, having different structural proteins, different cognate ligands and signal interactions. For example, a commercial Table of CD antigens lists this information. Species A, W, Z, AA-EE, GG and II have not been designated as CD antigens but have been shown to have distinct structural and functional features. For example, The Human Protein Reference Database describes the tissue expression patterns, structural and functional properties and any disease correlates for the receptors of species A, W, Z, AA-EE, GG and II.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 1 is generic as to species A-II.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6338. The examiner can normally be reached on 7:30-5:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

LAB